

Study of Clinical and Aetiological Profile of Neurological Manifestations in HIV Patients in a Tertiary Care Centre of Kumaon Region

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Abstract

Background: Neurologic manifestations affecting the nervous system at all levels and stages of HIV infection are common and increasing with the extended survival of HIV-positive persons. Neurological manifestations occur due to either primary pathologic process of HIV or secondary to opportunistic infection. The later stages of HIV cause severe immunodeficiency and render the patient susceptible to an array of neurological disorders, affecting virtually every component of the nervous system, and lead to considerable morbidity and mortality. The present study was conducted to study various neurological manifestations in HIV positive patients presenting to tertiary care centre of Kumaon region of Uttarakhand.

Methods: This was observational study of 100 HIV infected patients with clinical evidence of CNS involvement. A detailed clinical history and CNS examination was carried out. CD4 counts were measured and magnetic resonance imaging (MRI),

brain/electromyography, nerve conduction studies and cerebrospinal fluid (CSF) examination were done as required for diagnosis. Results were analyzed by using percentage and proportions whenever necessary.

Results: Tubercular meningitis was found to be the most common etiology among the patients 42(42%) followed by cryptococcal meningitis 14(14%), pyogenic meningitis 12(12%) and toxoplasmosis 6(6%). The commonest neurological presenting symptoms were headache (42%) and commonest abnormality found on neuroimaging was meningeal enhancement (24%).

Conclusions: High index of suspicion of neurological involvement in HIV patients in all stages helps in early diagnosis and timely institution of specific therapeutic treatment which in turn may considerably reduce the morbidity and mortality due to the disease.

Keywords: HIV positive patients, neurological manifestations, tubercular meningitis, cryptococcal meningitis, CIDP

Introduction

Since 2012, the confluence of knowledge on treatment and prevention of HIV infection has injected new enthusiasm in responses to the epidemic to shift the discourse to ending AIDS by 2030¹. Globally in 2016, there were about 37 million people living with HIV; about one million AIDS-related deaths and 1.8 million new HIV infections. About 70 percent of those living with HIV, dying or newly infected with HIV were from sub-Saharan Africa and notably in eastern and southern Africa. Today, with an estimated 5.134 million infections, India is home to the second largest population of people living with HIV and AIDS³.

Primary HIV infection is associated with clinical symptoms, primarily a mononucleosis syndrome, in about 50% of cases. In the ensuing 10 years, more than 50% of HIV-infected individuals develop the opportunistic infections (OIs) indicative of the onset of AIDS. Common presentations of AIDS include pneumonia, dysphagia, diarrhea, neurologic symptoms, fever, wasting, anemia, and vision loss⁴. HIV is neuroinvasive (can enter the central nervous system ((CNS)), neurotrophic (can live in neural tissues), and neurovirulent (causes disease of the nervous system). Presumed mechanisms of CNS invasion include the “Trojan horse” mechanism in which HIV-infected monocytes are admitted by the blood-brain barrier and mature into long-lived, persistently infected perivascular macrophages; infection of the choroid plexus; and direct infection of capillary endothelial cells, among others. HIV-infected cells include capillary endothelium, microglia, monocytes, macrophages, astrocytes, and choroid plexus.⁵

Neurologic manifestations affecting the nervous system at all levels and stages of HIV infection are common and increasing with the extended survival of HIV-positive persons. Neurological manifestations occur due to either primary pathologic process of HIV or secondary to opportunistic infection. The later stages of HIV cause severe immunodeficiency and render the patient susceptible to an array of neurological disorders, affecting virtually every component of the nervous system, and lead to considerable morbidity and mortality⁶.

The present study was conducted to study various neurological manifestations in HIV positive patients presenting to tertiary care Centre of kumaon region of uttarakhand.

Aims and Objectives

- To study the clinical and aetiological profile of HIV patients having neurological manifestations
- To find out spectrum of neurological manifestations in HIV patients and to correlate CD4 count with the same

Material and Methods

It was a Cross-sectional (observational) study done on all HIV patients attending medicine department with neurological manifestations. Patients with a confirmed status of HIV attending the OPD of department of general medicine with a sign of neurological manifestations were enrolled in the study after fulfilling the inclusion criteria. HIV status of the cases in the study was confirmed as per the guidelines of National AIDS control programme by detection of antibody on two successive samples using a third generation ELISA kit and if found positive a third sample is collected and tested using HIV-1/HIV-2 assay.

A thorough clinical history, clinical examination with socio demographic data, drug history, co-morbidities

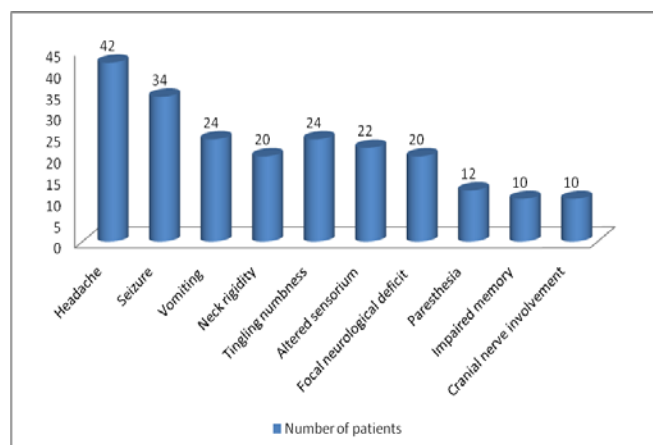
e.g., diabetes, alcohol abuse, drug abuse, epilepsy were noted. Routine haematological, biochemical investigations and CD4 counts were measured and magnetic resonance imaging (MRI) brain ,electromyography, nerve conduction studies and cerebrospinal fluid (CSF) examination were done as required for diagnosis. Results were analyzed by using percentage and proportions whenever necessary.

Proposed exclusion criterion were of Age <16 years ,Past history of neurological diseases,Diabetes,Alcohol and other drug abuse,Developmental problems and H/O neurobehavioral problems

Results

Headache and seizure were the most common neurological symptoms found to be present in 42% and 34% patients respectively followed by vomiting (24%), neck rigidity (20%), tingling numbness (24%), and altered sensorium (22%) respectively. Focal neurological deficit and paraesthesia were elicited in 20% and 12% respectively. Impairment in memory and cranial nerve abnormality were present in 10% of the cases.

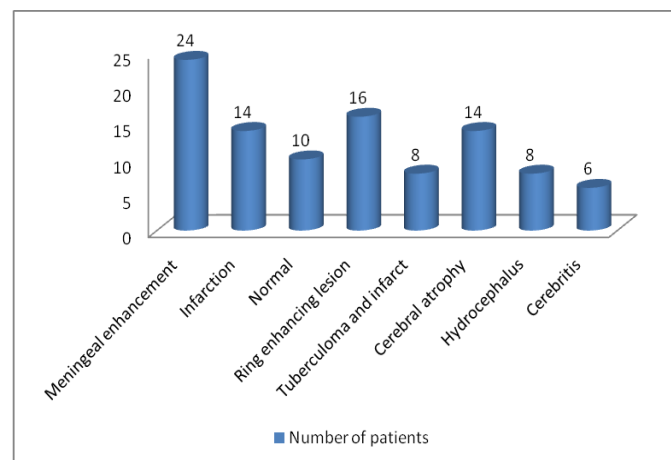
Figure 1: Distribution of neurological manifestations in patients



Meningeal enhancement and infarction were the most common neurological finding on CT/MRI found to be present in 24% and 14% patients respectively. Ring

enhancing lesion and cerebral atrophy were found to be present in 16% and 14% patients respectively. Tuberculoma and infarct was found to be present in 8(8%) patients. Hydrocephalus and Cerebritis were found to be present in 8(8%) and 6(6%) patients.

Figure 2 : Neurological findings on CT/MRI



Patients were classified into three groups on the basis of CD4 count

1. CD4 count ≤ 100 cells/mm²
2. CD4 count 101-200 cells/mm²
3. CD4 count > 200 cells/mm²

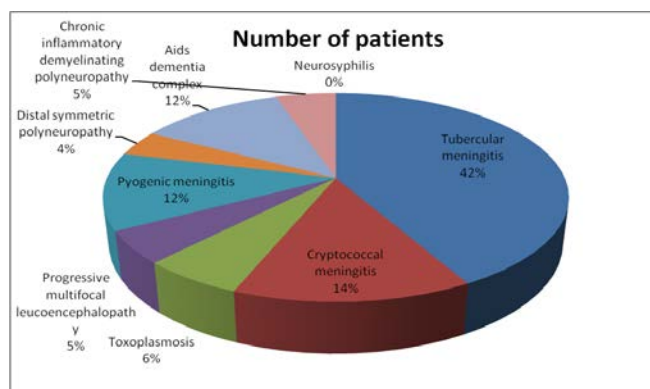
Maximum number of patients 45(45%) had CD4 count ≤ 100 cells/mm² . Only 27(27%) had CD4 count more than 200.

Table 1: Distribution of patients according to CD4 count /mm³

CD4 count /mm ³	Number of patients	Percentage of patients
≤ 100	45	45
101 to 200	28	28
>200	27	27
Total	100	100

Tubercular meningitis was found to be the most common etiology among the patients 42(42%) followed by cryptococcal meningitis 14(14%), pyogenic meningitis 12(12%) and toxoplasmosis 6(6%). Twelve

percent (12%) patients were diagnosed as AIDS dementia complex on the basis of clinical and radiological grounds. Progressive multifocal leucoencephalopathy, Chronic inflammatory demyelinating polyneuropathy and Distal symmetric polyneuropathy were diagnosed in 5(5%), 5(5%), and 4(4%) respectively. Neurosyphilis a rare entity, could not be found in any patient.



CD4 Count and Aetiological Diagnosis

Figure 3: Etiological distribution of patients

Table 2: Correlation of CD4 count with etiological diagnosis

Etiological diagnosis	Group 1 CD count/mm ² ≤ 100 (n = 45)	Group 2 CD count/mm ² 101-200 (n = 28)	Group 3 CD count/mm ² ≥ 200 (n = 27)	Total	p- value
Tubercular meningitis	20	12	10	42	0.00*
Cryptococcal meningitis	08	04	02	14	0.00*
Toxoplasmosis	04	02	00	06	0.01*
Progressive multifocal leucoencephalopathy	03	01	01	05	0.58
Pyogenic meningitis	06	04	02	12	0.06
Distal symmetric polyneuropathy	01	01	02	04	0.90
AIDS dementia complex	02	03	07	12	0.04*
Chronic inflammatory demyelinating polyneuropathy	01	01	03	05	0.48
Neurosyphilis	00	00	00	00	-

Discussion

In our study the mean age of the patients was 39.4 years. Majority of the patients belonged to the age group of 30 to 50 years. Mean age of the patients in a study conducted by Sonkar SK et al⁷ and Nagarjunakonda et al⁸ was 34.3 years and 38 years respectively. Seventy five (75%) percent of the patients of the present study were males while the remaining were females. Sixty nine (69%) patients in the present study were unmarried followed by 15 (15%) married and 16(16%) widow. Patients with neurological manifestations

62(62%) were not taking ART. Andrea Low et al⁹ explained about the substantial reduction in risk of OIs during the first year of ART, ranging from 57% to 91%. This was greatest for tubercular meningitis, cryptococcal meningitis and toxoplasmosis. The magnitude of effect of ART was more pronounced with the level of treatment adherence and immune recovery. There was also a non-statistically significant reduction for oesophageal candidiasis, herpes zoster, Kaposi sarcoma, and genital ulcer disease(GUD)⁹ Wadia RS et al¹⁰ and Gochitashvili N et al¹¹ correlated incidence of neurological findings with the immune status of HIV.

Fever was the most common extra neurological symptom in our study found to be present in 54(54%) patients followed by weight loss 45(45%), cough 40(40%) and diarrhea 35(35%) respectively. Lymphadenopathy and fungal infections including oral, topical infections were present in 15(15%) and 16(16%) respectively. Pain abdomen was the least common finding to be present in only 5(5%) patients. In a study conducted by Nagarjunakonda S et al⁸ fever was found to be present in 45 percent and 46 percent of the patients respectively. Munamala CSR et al¹² reported fever to be present in 71.2 percent of the patients.

In our study the most common neurological symptom found was headache present in 42(42%) patients followed by seizure 34(34%), vomiting 24(24%), tingling numbness 24(24%), altered sensorium 22 (22%) and neck rigidity 20 (20%) respectively. In a study conducted by Munamala CSR et al¹², Headache was the most common ailment followed by fever and vomiting (62.4%). Similar findings close to our study were also found in reports of Pal et al¹³

In the study conducted by Kausadikar SR et al¹⁴, most common neurological sign was signs of meningeal irritation (46%), followed by altered consciousness (26%) and hemiparesis (12%). Similarly a study done by Mansuri ZH et al¹⁵ revealed that the most common neurological sign was meningeal irritation (50%).

Meningeal enhancement and infarction were the most common neurological finding on CT/MRI found to be present in 24(24%) and 14(14%) patients respectively. Ring enhancing lesion and cerebral atrophy were found to be present in 16(16%) and 14(14%) patients. Tuberculoma and infarct was found to be present in 8(8%) patients. Hydrocephalus and Cerebritis was found to be present in 8(8%) and 6(6%) patients

respectively. In a study conducted by Kausadikar SR et al¹⁴, the most common abnormal finding on neuroimaging in patients presenting with neurological manifestation with HIV was meningeal enhancement found in 33% of the patients. Similarly, a study done by Rana HM et al¹⁶ the most common abnormal finding on neuroimaging in patients presenting with neurological manifestation with HIV was meningeal enhancement found in 46% of the patients.

Tubercular meningitis was encountered in 42(42%) patients followed by cryptococcal and pyogenic meningitis 14(14%) and 12(12%) patients respectively. Progressive multifocal leukoencephalopathy and toxoplasmosis were found to be present in 5(5%) and 6(6%) patients respectively. Distal symmetric polyneuropathy and chronic inflammatory demyelinating polyneuropathy were found to be present in 4(4%) and 5(5%) patients respectively.

Remaining patients who could not be diagnosed were integrated in AIDS dementia complex on clinical and radiological supporting evidences. They were 12(12%) in numbers. Neurosyphilis a rare entity could not be elicited in our study. Tuberculous meningitis followed by cryptococcal meningitis were the most common findings in the study conducted by Kausadikar SR et al¹⁴ which was comparable to a study done by Attili SV et al¹⁷ which also found the most common cause of headache to be tuberculous meningitis. A study done by Solu MD et al¹⁸ also revealed the most common HIV related secondary neurological illness to be TBM which is present in 34%.

Correlation between CD4 count, neurological manifestations and their etiologies

In the present study majority of patients 73(73%) were having CD4 count below 200cells/mm². Forty five

(45%) patients had CD4 counts less than 100 and 28(28%) had CD4 count between 101 – 200 cells/mm².

Tubercular Meningitis

Out of total 42(42%) patients of tubercular meningitis; 20(47.6%) patients were having CD4 count \leq 100cells/mm². The number of tubercular meningitis patients showed a declining trend with rise of CD4 count.

Cryptococcal Meningitis

Total 14(14%) patients of cryptococcal meningitis were found. Out of which 8(57%) patients were having CD4 count \leq 100cells/mm². Similar declining trend as shown by tubercular meningitis was shown by cryptococcal also.

Pyogenic Meningitis

Out of total 12(12%) patients of pyogenic meningitis; 06(50%) patients were having CD4 count \leq 100cells/mm². The number of pyogenic meningitis patients showed a declining trend with rise of CD4 count.

Toxoplasmosis

Out of total 06(06%) patients of toxoplasmosis; 04(66%) patients were having CD4 count \leq 100cells/mm². The number of toxoplasmosis patients showed a declining trend with rise of CD4 count.

Progressive Multifocal Leukoencephalopathy

Out of total 05(05%) patients of Progressive multifocal leukoencephalopathy; 03(60%) patients were having CD4 count \leq 100cells/mm². The number of Progressive multifocal leukoencephalopathy patients showed a declining trend with rise of CD4 count.

Aids Dementia Complex

Out of total 12(12%) patients of AIDS dementia complex; 02(16%) patients were having CD4 count \leq 100cells/mm² and; 07(58%) patients were having CD4

count \geq 200cells/mm². The number of AIDS dementia complex patients shows a rising trend with rise of CD4 count.

A trend of dominance of non-infective neurological involvement was seen with increased CD4 count and vice versa.

The correlation between CD4 count and tubercular meningitis(p<0.00*), cryptococcal meningitis(p<0.00*), toxoplasmosis(p<0.01*) and AIDS dementia complex(p<0.04*) were found to be statistically significant.(having p value less than 0.05; denoted by *) Mean CD4 count/mm³ among patients with Tubercular meningitis, Cryptococcal meningitis, Toxoplasmosis and Progressive multifocal leukoencephalopathy was found to be 145.8, 75.3, 78.9 and 143.8 respectively. Mean CD4 count/mm³ among patients with pyogenic meningitis, Distal symmetric polyneuropathy, AIDS dementia complex and Chronic inflammatory demyelinating polyneuropathy was found to be 96.2, 136.2, 163.4 and 159.8 respectively.

Our results were in concordance with the results obtained by Sharma SR et al¹⁹, who also reported similar findings in their study. In their study, most of patients with CNS infections had relatively low levels of CD4 counts i.e., <200/ μ l. CD4 count can serve as a guide to assess the HIV status, the risk for the development of neurological manifestations and help in instituting timely intervention in the form of prophylaxis and treatment.²⁰

Conclusion

According to our preliminary study, tubercular meningitis and cryptococcal meningitis are most prevalent infections in HIV population in our section of U.K. A larger, multicentre study to analyze the temporal trends of the neurological disease in HIV/AIDS patients in Indian population and its

changing profile is warranted. In addition, earlier HIV testing, diagnosis and proper follow-up, including primary prophylaxis for opportunistic infections and HAART, should be emphasized as public health policies for the treatment and prevention of AIDS in India and other developing countries

HIV is a pan neurological disease, affecting entire neuraxis without any exception. High index of suspicion of neurological involvement in HIV patients in all stages helps in early diagnosis and timely institution of specific therapeutic treatment which in turn may considerably reduce the morbidity and mortality due to the disease.

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